REMARKS

Claims 1-3, 5-6, and 10 are pending, claims 4, 7, and 8 having been canceled by the present amendment. Claims 1, 2, and 12 were amended to insert a reference to a SEQ ID NO, and is supported by disclosure at page 8, line 25, to page 9, line 4, of the specification. Claim 9 was amended to correct antecedent basis. News claim 24 and 25 were added; this claim is supported by disclosure at page 2, lines 1-3, of the specification.

No new matter has been added by this amendment.

35 U.S.C. § 112, first paragraph

Claims 1-12 were rejected for lack of written description. Claims 4, 7, and 8 were canceled. Independent claims 1, 2, and 12 were amended to add a reference to SEQ ID NO:2. The amended claims now recite the structure of an AFABP inhibitor. Therefore, the rejection for written description should be withdrawn.

The claims were also rejected for lack of enablement. The Examiner's grounds for rejection appear to be based on the position that "the state of the prior art for design of functional antisense for administration *in vivo* for the treatment effects was highly unpredictable." (page 10, lines 6-7, of Paper No.15).

The Examiner's rationale seems to suggest that methods for using antisense oligonucleotides to inhibit gene expression (or other activities), even if limited to a specific gene target, are not worthy of patent protection because of difficulties in the field. Although antisense methods may require further experimentation to optimize the desired result of reduced expression of a target gene, the methodology is well established and well accepted by the

scientific and medical community. Numerous antisense compositions are currently being administered to human subjects and antisense technology is regarded as a sound therapeutic approach.

The enablement standard permits some experimentation, so long as it is not undue. The difficulties described by the Examiner pertain to the general technology of antisense, rather than the specific invention claimed – use of AFABP antisense nucleic acids to inhibit tumor growth. Once a target gene has been identified, identification of optimal oligonucleotides is standard experimentation in the field of antisense technology. In the present case, Applicants made a significant contribution to the field of cardiovascular medicine by elucidating a molecular mechanism by which atherosclerotic lesions develop and by identifying a therapeutic target, AFABP. The amended claims are commensurate with the scope of the disclosure and their contribution to the field.

Optimization of AFABP oligonucleotides and confirming their inhibitory activity *in vivo* is well within the skill of a practitioner in the art of antisense technology. Given the description in the specification, evidence that a reduction in AFABP cooperssion inhibits macrophage differentiation and atherosclerotic lesion formation, and the copious information regarding making and using antisense oligonucleotides known in the art, Applicants submit that undue experimentation is not required to practice the invention as now claimed. Withdrawal of the rejections under §112 is respectfully requested.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicant submits that the pending claims are in condition for allowance. If there are any questions regarding these

amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for extension of time and a check in the amount of $930.00 is enclosed to cover the petition fee for a three month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21509-042.

Respectfully submitted,

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APPENDIX: MARKED-UP VERSION OF AMENDED CLAIMS

Cancel claims 4, 7, 8. Add new claims 24 and 25.

Amend claims 1, 2, 9, and 12 as follows.

1. A method of inhibiting formation of an atherosclerotic lesion comprising administering to a mammal a compound that reduces expression of AFABP, wherein said AFABP comprises the amino acid sequence of SEQ ID NO:4 and wherein a reduction in AFABP expression inhibits formation of an atherosclerotic lesion and wherein said compound comprises an nucleic acid comprising 10-100 nucleotides, the sequence of said nucleotides being complementary to a coding sequence of SEQ ID NO:2.

2. A method of inhibiting formation of an atherosclerotic lesion in a mammal, comprising identifying a mammal in need of said inhibition, and introducing to said mammal a compound that reduces expression of AFABP, wherein said AFABP comprises the amino acid sequence of SEQ ID NO:4 and wherein a reduction in AFABP expression inhibits formation of an atherosclerotic lesion and wherein said compound comprises an nucleic acid comprising 10-100 nucleotides, the sequence of said nucleotides being complementary to a coding sequence of SEQ ID NO:2.

9. The method of claim [7] 1, wherein said antisense nucleic acid is a DNA operatively linked to a macrophage-specific promoter, wherein transcription of said DNA yields nucleic acid product which is complementary to an mRNA encoding an AFABP polypeptide.

12. A method of inhibiting differentiation of a macrophage into a foam cell, comprising contacting said macrophage with an inhibitor of AFABP expression, wherein said AFABP comprises the amino acid sequence of SEQ ID NO:4 and wherein a reduction in AFABP expression inhibits differentiation of a macrophage into a foam cell and wherein said compound comprises an nucleic acid comprising 10-100 nucleotides, the sequence of said nucleotides being complementary to a coding sequence of SEQ ID NO:2.

Add new claims 24-25.

--24. (new) A method of inhibiting differentiation of a macrophage into a foam cell, comprising contacting said macrophage with an inhibitor of AFABP expression, wherein a reduction in AFABP expression inhibits differentiation of a macrophage into a foam cell and wherein said inhibitor comprises a compound that binds to a cis-acting regulatory sequence of AFABP, said inhibitor comprising a peroxisome proliferator-activated receptor gamma (PPARγ) or peroxisome proliferator-activated receptor alpha (PPARα) compound.--

--25. (new) A method of inhibiting formation of an atherosclerotic lesion comprising administering to a mammal a compound that reduces expression of AFABP, wherein said inhibitor comprises a compound that binds to a cis-acting regulatory sequence of AFABP, said inhibitor comprising a peroxisome proliferator-activated receptor gamma (PPARγ) or peroxisome proliferator-activated receptor alpha (PPARα) compound.--